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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,259	07/21/2004	Patrick, Arnoldus, Maria Van Buggenum	0-2002.712 US	9811
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ORGANON USA, INC. c/o Schering-Plough Corporation 2000 Galloping Hill Road Mail Stop: K-6-1, 1990 Kenilworth, NJ 07033			EXAMINER BADJO, BARBARA P	
			ART UNIT 1612	PAPER NUMBER
			NOTIFICATION DATE 08/25/2009	DELIVERY MODE ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

jill.corcoran@spcorp.com  
patents@spcorp.com

# Office Action Summary

**Application No.**

10/502,259

**Applicant(s)**

VAN BUGGENUM ET AL.

**Examiner**

Barbara P. Badio

**Art Unit**

1612

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-9 and 11 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-9 and 11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SF/ICE)  
Paper No(s)/Mail Date \_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_.

**Final Office Action on the Merits**

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

***Status of the Application***

2. Claims 1-9 and 11 are pending in the present application and are rejected as indicated below.

***Claim Rejections - 35 USC § 103***

3. **The rejection of claims 1-9 under 35 USC 103(a) over Babcock et al. (US 3,341,557) and Campbell et al. (Steroids, 1963).**

Applicant argues the prior art does not indicate that protection of the 17-hydroxyl group is preferred or that it would result in a better yield of the desired 7 $\alpha$ -methyl derivatives. According to applicant, the suggestion made by Campbell in 1963 that the introduction of a 7 $\alpha$ -methyl substituent can be effected selectively and in good yield to give predominantly the 7 $\alpha$ -methyl epimer is not related to a reaction with a starting material wherein the hydroxyl group is protected by an acetate group. Applicant also argues the protection of the 17-hydroxyl group with a trialkyl silyl group results in a markedly improved stereoselectivity of the Grignard reaction in favor of the desired 7 $\alpha$ -methyl isomer. Lastly, applicant argues (a) '393 does not teach or suggest that in steroid chemistry wherein 4,6-diene-ketone compounds are reacted with a methyl

Grignard reagent a trialkyl silyl group protecting group is preferred and has significant advantages over a free hydroxyl group or an acetate protecting group and (b) a side-by-side comparison shows a greater yield of the desired protected product utilizing a starting material wherein the 17-hydroxyl group is protected with a silyl group versus when an unprotected 17-hydroxyl starting material was utilized. Applicant's argument was considered but not persuasive for the following reasons.

First, the issue is not whether the prior art teaches a preference for the protection of the 17-hydroxyl group over the free alcohol. The issue is whether the use of a 17-hydroxyl protected group is made obvious by the prior art. Both Babcock and Campbell teach the process will run to completion with the production of the desired 7 $\alpha$ -methyl-4-ene-3-ketone derivative utilizing a 17-hydroxyl protected starting material such as a 17-acetate 4,6-diene-3-ketone steroid. The only difference between the process taught by the prior art, such as Babcock or Campbell, and the claimed invention is the hydroxyl protected group utilized.

Applicant argues the selectivity taught by Campbell is not related to a reaction with a starting material wherein the hydroxyl group is protected by an acetate group. The Office agrees that Campbell does not teach that the selectivity is related to the protection of the starting material. What Campbell teaches is *"the introduction of a 7 $\alpha$ -methyl substituent depends on the observation that 1,6-addition of the methyl Grignard reagent to a  $\Delta^{4,6}$ -3-ketone can be effected selectively and in good yield in the presence of a cuprous salt to give predominantly the 7 $\alpha$ -methyl epimer"*. In other words, the selective production of 7 $\alpha$ -methyl 4-ene-3-ketone steroid derivative utilizing the

corresponding 7-acetate 4,6-diene-3-ketone steroid in the presence of methyl Grignard reagent and a cuprous salt. Again, the only difference between the prior art process and the claimed process is the 17-hydroxyl protection group of the starting material.

Applicant also argues (a) '393 does not teach the use of a trialkyl silyl group is preferred or has significant advantages over the use of the free hydroxyl group or an acetate in the process and (b) the protection of the 17-hydroxyl group with a trialkyl silyl group would result in a markedly improved stereoselectivity of the Grignard reaction in favor of the desired 7 $\alpha$ -methyl isomer.

As noted in the previous Office Action, '393 was utilized to show that which is well known in the art, i.e., acyl and trialkyl silyl groups are both well known hydroxyl protecting groups. According to MPEP §2144.06, substituting art-recognized equivalents for a known purpose is *prima facie* obvious, and "an express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious." *In re Fout*, 675 F.2d 297, 213 USPQ 532 (CCPA 1982). The substitution of one hydroxyl protecting group for another in the prior art process would have been obvious to one of ordinary skill in the art at the time of the present invention.

Lastly, the examiner disagrees that Campbell teaches the result, i.e., yield, obtained with an unprotected 17-hydroxyl group is comparable to the use of an acetate protecting group. What the prior art teaches is that the process will run to completion with the production of the desired end product whether the 17-hydroxyl group is unprotected or protected with an acyl group not that the yield would be comparable. If applicant's argument is that the use of a trialkyl silyl group in the process as taught by

the prior art results in unexpected/unobvious results, a comparison of the claimed trialkyl silyl group and the prior art acyl group, i.e., acetate group, in the process under identical conditions is necessary. The only difference in said experiments should be in the hydroxyl protected group of the starting material.

For these reasons and those given in the previous Office Action, the rejection of claims 1-9 under 35 USC 103(a) over Babcock et al. (US 3,341,557) and Campbell et al. (Steroids, 1963).

**4. The rejection of claim 11 under 35 USC 103(a) over Babcock et al. (US 3,341,557) and Campbell et al. (Steroids, 1963) as applied to claims 1-9 above, and further in view of Peters et al. (WO 01/58919) is maintained.**

Applicant argues Peters teaches  $7\alpha$ -alkylation using a lower alkyl lithium in the presence of lithium bromide wherein the hydroxyl moiety is protected with a suitable protecting group. Applicant's argument was considered but not persuasive for the following reason.

As noted in the previous Office Action, the use of analogous reactants in a known process is prima facie obvious. Like Campbell and Babcock, Peter teaches the production of  $7\alpha$ -methyl derivatives from the corresponding 4,6-diene-3-ketone steroids. Based on what the prior art teaches and the level of skill of the ordinary artisan in the art at the time of the present invention, it would have been obvious to the skilled artisan in the art at the time of the present invention that (a) the process taught by Babcock and Campbell would run to completion with the utilization the 4,6-dienes of Peters as the

starting material and the production of the desired/corresponding end product or (b) the substitution of the reagents of Campbell and Babcock in the process of Peters would result in the production of the desired 7 $\alpha$ -methyl compounds.

For these reasons and those given in the previous Office Action, the rejection of claim 11 under 35 USC 103(a) over Babcock et al. (US 3,341,557) and Campbell et al. (Steroids, 1963) as applied to claims 1-9 above, and further in view of Peters et al. (WO 01/58919) is maintained.

**5. The rejection of claim 10 under 35 USC 103(a) over Peters et al. (WO 01/58919) is made moot by the cancellation of the instant claim.**

### ***Conclusion***

**6. THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Telephone Inquiry***

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Barbara P. Badio whose telephone number is 571-272-0609. The examiner can normally be reached on M-F from 6:30am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Barbara P. Badio/  
Primary Examiner, Art Unit 1612